

MEDTOX[®]

DIAGNOSTICS, INC.

PROFILE[®]-III ER PACKAGE INSERT

The PROFILE[®]-III ER products are one-step qualitative screening assays for the detection of one or more of the following: Amphetamine, Barbiturates, Benzodiazepines, Cocaine, Methamphetamine/ 3,4 Methylenedioxymethamphetamine, Methadone, Opiates, Phencyclidine, Propoxyphene, THC (Cannabinoids), and Tricyclic Antidepressants and or their metabolites in human urine. **All PROFILE[®]-III ER product(s) are covered by this insert. Refer to product labeling for the actual drugs assayed by the kit or system configuration.**

The Lateral Flow (LatFlo[®]) Adulterant Strip (LFAS) is a one-step qualitative screening assay for the detection of Oxidants and Nitrites and the Determination of Specific Gravity and pH Values in human urine. It is used to evaluate specimens for adulteration prior to Drugs of Abuse urine (DAU) testing. The LFAS strip is only for Forensic/Toxicology use and not for in vitro diagnostic applications. **The LFAS test strip is only contained in products labeled with "LFAS" on the label.**

1. INTENDED USE

The PROFILE[®]-III ER Drugs of Abuse Test is a one-step immunochromatographic test for the rapid, qualitative detection of one or more of the following: Amphetamine, Barbiturates, Benzodiazepines, Cocaine, Methamphetamine/ 3,4 Methylenedioxymethamphetamine, Methadone, Opiates, Phencyclidine, Propoxyphene, THC (Cannabinoids), and Tricyclic Antidepressants in human urine. It is not for over-the-counter sale. The test detects drug classes at the following cutoff concentrations:

AMP	Amphetamine (d-Amphetamine)	1000 ng/mL	OPI2	Opiates (Codeine/Morphine)	2000 ng/mL
BAR	Barbiturates (Butalbital)	200 ng/mL	OPI3	Opiates (Codeine/Morphine)	300 ng/mL
BZO	Benzodiazepines (Nordiazepam)	300 ng/mL	PCP	Phencyclidine (Phencyclidine)	25 ng/mL
COC	Cocaine (Benzoyllecgonine)	300 ng/mL	PPX	Propoxyphene (Norpropoxyphene)	300 ng/mL
MAMP	Methamphetamine (d-Methamphetamine)	1000 ng/mL	THC	Cannabinoids (11-nor-9-carboxy- Δ^9 -THC)	50 ng/mL
MDMA	3,4 Methylenedioxymethamphetamine	1500 ng/mL	TCA	Tricyclic Antidepressants (Desipramine)	300 ng/mL
MTD	Methadone (Methadone)	300 ng/mL			

THE PROFILE-III ER DRUGS OF ABUSE TEST PROVIDES ONLY A PRELIMINARY ANALYTICAL TEST RESULT. A MORE SPECIFIC ALTERNATE CHEMICAL METHOD MUST BE USED IN ORDER TO OBTAIN A CONFIRMED ANALYTICAL RESULT. GAS CHROMATOGRAPHY/ MASS SPECTROMETRY (GC/MS) OR HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) IS THE PREFERRED CONFIRMATORY METHOD. CLINICAL CONSIDERATION AND PROFESSIONAL JUDGMENT SHOULD BE APPLIED TO ANY DRUG OF ABUSE TEST RESULT, PARTICULARLY WHEN PRELIMINARY POSITIVE RESULTS ARE OBTAINED.

2. SUMMARY AND EXPLANATION OF THE TEST

Qualitative PROFILE-III ER Drugs of Abuse screens utilize a one-step, solid-phase immunoassay technology to provide a very rapid test requiring no instrumentation. This test may be used to screen urine samples for one or more of the following drug classes prior to confirmatory testing:

The "Amphetamines" are a group of drugs that are central nervous system stimulants. This group includes 'amphetamine' and 'methamphetamine', and related designer drugs like '3,4 Methylenedioxymethamphetamine', (better known as Ecstasy or MDMA, a psychoactive drug with hallucinogenic effects).

The drug 'Amphetamine' (d-amphetamine) is detected on the device only at the (AMP) position. Both the designer drug Ecstasy (MDMA) 'Methylenedioxymethamphetamine' and methamphetamine (d-methamphetamine) are detected on the device at the (MAMP) position. The (MAMP) antibody does not differentiate between methamphetamine and ecstasy.

Barbiturates (BAR) are a group of structurally related prescription drugs that are used to reduce restlessness and emotional tension, induce sleep and to treat certain convulsive disorders.

Benzodiazepines (BZO), a group of structurally related central nervous system depressants, are primarily used to reduce anxiety and induce sleep.

Cocaine (COC) is a central nervous system stimulant. Its primary metabolite is benzoyllecgonine.

Methadone (MTD) is a synthetic opioid used clinically as a maintenance drug for opiate abusers and for pain management.

Opiates (OPI) are a class of natural and semi-synthetic sedative narcotic drugs that include morphine, codeine and heroin.

Phencyclidine (PCP) is a hallucinogenic drug.

Propoxyphene (PPX) is a narcotic analgesic. It's primary metabolite is norpropoxyphene.⁶

Marijuana (THC) is a hallucinogenic drug derived from the hemp plant. Marijuana contains a number of active ingredients collectively known as Cannabinoids.

Tricyclic Antidepressants (TCA) are a group of structurally related prescription drugs that are used to manage depression.

Many factors influence the length of time required for drugs to be metabolized and excreted in the urine. A variety of factors influence the time period during which drug metabolites are detected in urine; the rate of urine production, the volume of fluid consumption, the amount of drug taken, the urine pH, and the length of time over which drug was consumed. Drinking large volumes of liquid or using diuretics to increase urine volume will lower the drug concentration in the urine and may decrease the detection period. Although the detection period for these drugs varies widely depending upon the compound taken, dose and route of administration and individual rates of metabolism, some general times have been established and are listed below.¹⁴

<u>Drug</u>	<u>Detection Period</u>	<u>Drug</u>	<u>Detection Period</u>
Amphetamine		Opiates	
Acid Conditions	1-3 days	Heroin	1 day
Alkaline Conditions	3-10 days	Morphine	1-3 days
		Codeine	1-3 days
Barbiturates		PCP	
Short-Acting	up to 6 days	Single Use	7-8 days
Long-Acting	up to 16 days	Chronic Use	2-4 weeks
Benzodiazepines	1-12 days	Propoxyphene	up to 1 week
Cocaine	1-3 days	THC	
		Single Use	1-3 days
Methamphetamine/MDMA		Chronic, Light Use	3-29 days
Acid Conditions	1-3 days	Chronic, Heavy Use	Up to 12 weeks
Alkaline Conditions	3-10 days		
Methadone	1-3 days	Tricyclic Antidepressants	1-7 days

The LFAS is a lateral flow strip with impregnated reagent test pads that detect specific analytes in human urine. The analytes detected are Oxidants and Nitrites. The strip also approximates the pH and specific gravity values. Urine samples with 'abnormal' values should be submitted to a reference laboratory for additional testing.

Oxidants The detection is based on the oxidative activity of compounds (e.g. chromate salts and/or Bleach) that catalyze the oxidation of an indicator by an organic hydroperoxide producing a blue/orange color. The color intensity is directly proportional to the concentration of Oxidants present in the sample and is observed visually and compared to the color comparator chart to obtain a result.

Nitrites The test is based on the principles of the Griess reaction for the detection of Nitrites. The test pad contains an amine and a coupling component. A red/orange colored azo compound is obtained by diazotization and subsequent coupling. The color intensity is directly proportional to the concentration of Nitrites present in the sample and is observed visually and compared to the color comparator chart to obtain a result.

pH The test paper contains indicators that change colors between pH 2 and pH 11. The color scale gives an approximate indication for pH values between those levels.

Specific Gravity The test pad reacts with ions in urine to indicate concentrations from 1.000 to 1.020. The color changes range from dark green with low ionic concentrations through green to yellow/orange in urines with high ionic concentrations. The color is observed visually and compared to the color comparator chart to obtain an approximate result.

3. PRINCIPLES OF THE PROCEDURE

The PROFILE-III ER Drugs of Abuse Test is a one-step, competitive, membrane-based immunochromatographic assay. A single urine sample can be evaluated for the presence of each of the specified classes of drug(s) in a single device. The device consists of antibody-colloidal gold, drug-conjugates and a control line.

1. ANTIBODY-COLLOIDAL GOLD Mouse monoclonal drug antibodies were developed. Each antibody only binds drug(s) from the drug class tested. Antibody-colloidal gold solutions were prepared by absorbing each of the individual monoclonal antibodies to colloidal gold. The colloidal gold solutions were applied to the sample well pad in the drugs of abuse test.

2. DRUG-CONJUGATES Drug from the class tested was individually conjugated to bovine serum albumin (BSA) or IgG. Each drug conjugate was immobilized as a line at a labeled location on the membrane strip.

3. CONTROL LINE Each test strip has anti-mouse immunoglobulin antibody immobilized as a line on the membrane at the CTRL location on the device window. The anti-mouse immunoglobulin antibody can bind to any of the mouse antibodies coated on the colloidal gold.

The device can be used to detect specific class(es) of drug(s) in urine because drug(s) in the urine and the drug(s) conjugated to the protein compete to bind to the antibody-colloidal gold in a highly specific reaction. When the urine sample is placed in the sample well(s), the dried antibody-colloidal gold on the sample pad(s) dissolves and the urine wicks up the white strips carrying the reddish-purple antibody-colloidal gold as a solution with it.

Negative Samples

When no drug(s) is present in the urine sample, the reddish purple antibody-colloidal gold solutions migrate along the strip then binds to the appropriate drug conjugate immobilized on the membrane. The binding of the antibody-colloidal gold to the drug conjugate generates an easily visible reddish-purple line at the appropriate "T" location on the device. Strips with two tests will be labeled with two colors and are on left-hand side of device. The top color will indicate the T1 test with T1= drug test name. The bottom color will indicate the T2 test with T2= drug test name. Strips with only one color will have test results appear at the T1 position. Negative results can be reported as soon as a line is visible.

Positive Samples

When drug(s) is present in the urine sample the antibody-colloidal gold binds to the drug(s) before it migrates along the strip. However, when the antibody-colloidal gold binds to the drug(s) in the urine, the antibody colloidal gold cannot bind to the drug conjugate immobilized on the membrane. When the drug concentration is at or above the cutoff concentration, the majority of the antibody-colloidal gold is bound to the drug from the urine. Therefore, as the drug bound antibody-colloidal gold migrates along the strip(s), it is unable to bind to the appropriate drug conjugate immobilized on the membrane. Therefore no line is generated at the "T" location for a positive sample. Read positive results at 5 minutes. The control line should be present for the test to be valid. The test must be read within 15 minutes of the sample application. The test result after 15 minutes may not be consistent with the original reading.

CTRL Line

Each test strip has an internal procedural control. A line must form at the Control "C" location on the device to indicate that the reagents are migrating properly. If a Control line does not form, the test is considered invalid. A Control line forms when the antibody-colloidal gold binds to the anti-mouse immunoglobulin antibody immobilized on the membrane at the "C" location(s) on the device.

4. MATERIALS PROVIDED/STORAGE CONDITIONS

Each PROFILE-III ER Drugs of Abuse Test contains all the reagents necessary to test one urine sample simultaneously for one or more drugs.

- The test device contains one or more test strips composed of a membrane strip coated with drug conjugate and a pad coated with antibody dye complexes in a protein matrix.
- The test device may contain a membrane strip laminated with Adulterant test pads for testing the presence of Oxidants and Nitrites, as well as determining approximate values of Specific Gravity and pH in human urine. **The LFAS test strip is not** contained in every PROFILE-III ER product.

Kit Contents

- Twenty-five (25) test devices in individual foil packages and twenty-five (25) transfer pipettes.

2. One reference guide.
3. For LFAS products only, five color comparator charts.

Storage Conditions

The kit, in its original packaging, should be stored at 2-25°C (36-77°F) until the expiration date on the label.

5. PRECAUTIONS

1. Urine specimens and all materials coming in contact with them should be handled and disposed of as if infectious and capable of transmitting infection. Never pipette by mouth and avoid contact with broken skin.
2. Avoid cross-contamination of urine samples by using a new urine specimen container and pipette for each urine sample.
3. The device should remain in its original sealed foil pouch until ready to use. If the pouch is damaged, do not use the test.
4. Do not store the test kit at temperatures above 25°C (77°F).
5. If devices have been stored refrigerated, bring to ambient temperature (18-25°C/ 64-77°F) prior to opening foil pouch.
6. Do not use tests after the expiration date printed on the package label.
7. The drug screen portion of the device is for in vitro diagnostic use only. The LFAS strip is for Forensic/Toxicology use only.

6. SAMPLE COLLECTION AND PREPARATION

The urine sample should be collected in a clean glass or plastic container. Collection of 45 mL of urine is more than sufficient for initial and subsequent testing. No preservatives should be added. Urine may be tested immediately following collection. The specimen may be refrigerated if testing is going to be delayed for more than a day. Urine may be frozen for longer storage. Stored urine must be brought to ambient temperature (18 to 25°C/64 to 77°F) and mixed well to assure a homogeneous sample prior to testing.

7. MATERIALS REQUIRED BUT NOT PROVIDED

1. Urine collection container.

NOTE: Specimen containers, disposable gloves and urine temperature strips are available from MEDTOX Diagnostics, Inc.

8. TEST PROCEDURE

1. Open one pouch for each sample to be tested and label the device with the patient or sample identification (ID).
2. To run the test device
 - Hold device in hand at about a 60° angle.
 - Refer to the package labeling (# of tests) and the Urine Sample Volume table below to determine the volume needed to run your device.

Urine Sample Volume			
# of Tests	# of Strips	Pipette Mark	Volume
12	9	Base of Bulb	650µl
9	7	0.5ml	500µl
5 & 7	4 & 5	0.3ml	300µl

- Add the appropriate sample volume into the sample well with the transfer pipette supplied.
- Tilt the device from side to side to distribute urine evenly across test strips. Test reagents will start migrating up the strips & lines will begin to develop.
- Hold the device until the reddish-purple control lines have formed across the test strips at the "C" position (about 40 sec).
- Once the control lines have formed, lay the device flat and read after 5 minutes.

9. READING THE TEST RESULTS

Negative: The appearance of a reddish-purple line at both the control area (C) and appropriate test area (T) indicates a negative test result. **The color intensities of the control lines (C) and test lines (T) may not be equal and may vary from test to test. The test line and control line positions may vary slightly from test strip to test strip. Any line of faint color intensity indicates a negative test result.**

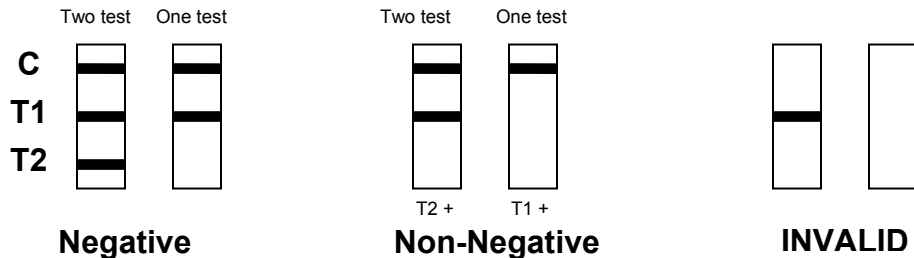
Non-Negative: The appearance of a control line and the absence of a test line indicate a preliminary positive test result for that drug.

Invalid: The control line must be present for the test to be valid. The absence of a control line indicates the test is invalid. The urine sample should be retested on a new device.

10. INTERPRETATION OF TEST RESULTS

A **NEGATIVE** test result for a specific drug indicates that the sample does not contain the drug/drug metabolite above the cutoff level.

A **NON-NEGATIVE** test result for a specific drug indicates that the sample may contain drug/drug metabolite near or above the cutoff level. It does not indicate the level of intoxication or the specific concentration of drug in the urine sample. Examples of Negative and Non-Negative results are shown below.



There are other possible results depending on the drug or combination of drugs present in the urine sample.

11. QUALITY CONTROL

An internal procedural control is included on each device. A line must form at the Control (C) location on the device to indicate that the proper sample volume was used and that the reagents are migrating properly. If a Control line does not form, the test is considered invalid. The Control line consists of immobilized anti-mouse antibody that reacts with the antibody-colloidal gold as it passes this region of the membrane. Formation of a visible line verifies the Control line antibody antigen reaction occurred. This line may be considered an internal negative procedural control. In addition, if the test has been performed correctly and the device is working properly, the background will clear such that result lines are distinct. The cleared background may be considered an internal positive procedural control. The visible Control line (C) should always be present regardless of whether drug is absent or present in the sample.

The purpose of quality control in laboratory testing is to ensure accuracy, reliability of results and to detect errors. Because the devices are self-contained, single use tests, traditional quality control programs do not apply. The Quality Control program MEDTOX recommends for these non-instrumented test devices includes a combination of the internal device controls and external controls to ensure accuracy, reliability and to detect possible errors. The on-board reactive device controls may be one aspect of the quality program utilized by a laboratory to satisfy the daily quality control requirement established by the Laboratory Director. Another aspect of a quality control program includes an external negative control containing no drug and a positive drug control challenging to the assay cutoff concentration. These controls may be used to initially test each shipment of product received by the laboratory or to verify appropriate storage conditions and long-term stability of the test reagent. To follow good laboratory practices, we recommend that the user document the receipt of each new lot number of devices, the results of external controls performed initially and periodically thereafter, and the results of the internal controls within each device.

It is the responsibility of each Laboratory Director to demonstrate and document the validity of the alternate QC procedure they choose to use in their laboratory. For additional information or forensic and workplace testing requirements, users should contact and follow the appropriate federal, state, and local guidelines. Quality control materials are available from MEDTOX and commercial sources. Contact MEDTOX for further information.

12. LIMITATIONS OF THE PROCEDURE

1. The PROFILE-III ER Drugs of Abuse Test is only for use with unadulterated human urine samples. Urine samples which are either extremely acidic (below pH 4.0) or basic (above pH 9.0) may produce erroneous results.
2. A positive result for any drug(s) does not indicate or measure intoxication. It only indicates the presence of specific drug(s) in the urine specimen.
3. Test results interpreted after 15 minutes may not be consistent with the original result obtained at 5 minutes.
4. The PROFILE-III ER Drugs of Abuse Test was not evaluated in point-of-care settings.
5. There is a possibility that other substances and/or factors, e.g. technical or procedural errors, may interfere with the test and cause false results.

LFAS Strip

The purpose of the adulteration strip is to screen for abnormal conditions in human urine samples, such as dilution or the addition of drug-test interfering substances. Occasionally medications may discolor the urine, and make it difficult to read the result. When in doubt send the urine sample to a reference laboratory for additional testing.

Oxidant

Nitrites, acting as oxidizing agents in solution, will produce a blue/green color change on the Oxidant pad.

Nitrite

Abnormal results can be caused by the presence of diagnostic or therapeutic dyes in the urine. Very high concentrations of oxidant such as 80% bleach will produce a brown color change on the Nitrite pad.

13. EXPECTED VALUES

The Substance Abuse and Mental Health Services Administration (SAMHSA) recommends the following screening test cutoffs:

AMP	Amphetamine	1000 ng/mL
COC	Benzoylcegonine	300 ng/mL
MAMP	Methamphetamine	1000 ng/mL
OPI	Morphine and Codeine	2000 ng/mL
PCP	Phencyclidine	25 ng/mL
THC	11-nor-9-carboxy- Δ^9 -THC	50 ng/mL

There are no SAMHSA recommended screening levels for barbiturates, benzodiazepines, methadone, MDMA, propoxyphene and tricyclic antidepressants and/or their metabolites.

The PROFILE-III ER Drugs of Abuse Test qualitatively detects amphetamines, barbiturates, benzodiazepines, cocaine, methamphetamine/MDMA, methadone, opiates, phencyclidine, propoxyphene, THC, and tricyclic antidepressants and/or their metabolites as listed (See Specificity).

LFAS Test:

Urine that produce an abnormal result on the LFAS adulteration strip should be sent to a reference laboratory for more definitive testing to determine if the urine may be dilute, substituted, invalid and/or adulterated.

14. PERFORMANCE CHARACTERISTICS

Sensitivity

The PROFILE-III ER Drugs of Abuse Test detects one or more of the following drugs at cutoff levels listed below. Cutoffs for amphetamines, cocaine metabolite, methamphetamines, opiates (OPI2), phencyclidine, and cannabinoids (THC) are based on SAMHSA recommendations for screening of these drugs in human urine³. The Opiate (OPI3) test, if present, detects opiates below the SAMHSA recommendations for screening of opiates in human urines. There are no SAMHSA recommended screening cutoff levels for barbiturates, benzodiazepines, MDMA, methadone, Propoxyphene, Norpropoxyphene, and Tricyclic Antidepressants.

AMP	Amphetamine	1000 ng/mL
BAR	Barbiturates (Butalbital)	200 ng/mL
BZO	Benzodiazepines (Nordiazepine)	300 ng/mL
COC	Benzoylcegonine	300 ng/mL
OPI2	Morphine and Codeine	2000 ng/mL
OPI3	Morphine and Codeine	300 ng/mL
MAMP	Methamphetamine	1000 ng/mL
MDMA	Methylenedioxyamphetamine	1500 ng/mL
MTD	Methadone (Methadone)	300 ng/mL
PCP	Phencyclidine	25 ng/mL
PPX	Propoxyphene (Norpropoxyphene)	300 ng/mL
THC	11-nor-9-carboxy- Δ^9 -THC	50 ng/mL
TCA	Tricyclic Antidepressants (Desipramine)	300 ng/mL

Accuracy

A panel of naturally metabolized urine samples for the following drug(s) was analyzed using the PROFILE-III ER Drugs of Abuse Test and the Boehringer Mannheim qualitative CEDIA[®] assay or the ROCHE ABUSCREEN ONLINE[®] for each drug and the results were compared. Results are shown in the following tables.

**ACCURACY COMPARED TO THE BOEHRINGER MANNHEIM QUALITATIVE CEDIA[®]
or THE ROCHE ABUSCREEN ONLINE[®] II ASSAYS**

CEDIA AMPHETAMINE (1000 ng/mL cutoff)

PROFILE-III ER AMP (1000 ng/mL cutoff)		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
	Positive	64	0	64
	<u>Negative</u>	<u>2</u>	<u>618</u>	<u>620</u>
	Total	66	618	684

Overall agreement: >99% (682/684). Samples having discrepant results were analyzed by GC/MS. The two false negative samples contained amphetamine at 2353 and 3569 ng/mL.

CEDIA COCAINE (300 ng/mL cutoff)

PROFILE-III ER COC (300 ng/mL)		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
	Positive	96	8	104
	<u>Negative</u>	<u>2</u>	<u>578</u>	<u>580</u>
	Total	98	586	684

Overall agreement: 99% (674/684). Samples having discrepant results were analyzed by GC/MS. Of the eight false positive samples one contained 151 ng/mL while seven did not contain cocaine metabolite detectable at the GC/MS cutoff of 150 ng/mL. The two false negative samples contained cocaine metabolite at 688 and 666 ng/mL.

ROCHE ABUSCREEN ONLINE[®]-II OPIATE (2000 ng/mL cutoff)

PROFILE-III ER OPI (2000 ng/mL cutoff)		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
	Positive	68	0	68
	<u>Negative</u>	<u>0</u>	<u>89</u>	<u>89</u>
	Total	68	89	157

Overall agreement: 100% (157/157).

CEDIA OPIATE (300 ng/mL cutoff)

PROFILE-III ER OPI (300 ng/mL cutoff)		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
	Positive	133	1	134
	<u>Negative</u>	<u>0</u>	<u>550</u>	<u>550</u>
	Total	133	551	684

Overall agreement: >99% (683/684). The discrepant sample was analyzed by GC/MS. The one false positive sample did not contain morphine or codeine detectable at the GC/MS cutoff of 300 ng/mL.

CEDIA PHENCYCLIDINE (25 ng/mL cutoff)

PROFILE-III ER PCP (25 ng/mL)		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
	Positive	56	2	58
	<u>Negative</u>	<u>1</u>	<u>625</u>	<u>626</u>
	Total	57	627	684

Overall agreement: >99% (681/684). Samples having discrepant results were analyzed by GC/MS. The two false positive samples did not contain phencyclidine detectable at the GC/MS cutoff of 25ng/mL. The one false negative sample contained phencyclidine at 28 ng/mL.

CEDIA MULTI-LEVEL THC (50 ng/mL cutoff)

PROFILE-III ER THC (50 ng/mL cutoff)		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
	Positive	194	3	197
	<u>Negative</u>	<u>10</u>	<u>477</u>	<u>487</u>
	Total	204	480	684

Overall agreement: 98% (671/684). Samples having discrepant results were analyzed by GC/MS. The three false positive samples were found to contain 16, 28, and 32 ng/mL while the ten false negative samples contained 32, 35, 41, 42, 46, 46, 49, 50, 50, and 90 ng/mL.

**RELATIVE SENSITIVITY AND SPECIFICITY COMPARED TO THE BOEHRINGER MANNHEIM
QUALITATIVE CEDIA[®] or THE ROCHE ABUSCREEN ONLINE[®] II ASSAYS
(Amphetamines, Cocaine, Opiates, PCP and THC)**

<u>Relative Sensitivity</u>	<u>Relative Specificity</u>
AMP 97% (64/66)	100% (618/618)
COC 98% (96/98)	99% (578/586)
OPI2 100% (68/68)	100% (89/89)
OPI3 100% (133/133)	>99% (550/551)
PCP 98% (56/57)	>99% (625/627)
THC 95% (94/204)	99% (477/480)

ACCURACY COMPARED to GC/MS

		<u>PROFILE-III ER</u>	<u>GC/MS</u>	<u>Values for Discrepant Samples (ng/mL)</u>
AMP	Positive	48	50	
	Negative	52	50	2353 and 3569
COC	Positive	49	50	
	Negative	51	50	666
OPI2	Positive	47	47	
	Negative	0	0	No Discrepant
OPI3	Positive	50	50	
	Negative	50	50	No Discrepant
PCP	Positive	49	50	
	Negative	51	50	28
THC	Positive	48	50	
	Negative	52	50	35 and 46

Precision (Amphetamines, Cocaine, Opiates, PCP, and THC)

Performance around the specific cutoff for each drug was measured by testing standard drug solutions diluted in drug-free urine in replicates of 20 each on 3 different days by 3 operators. Twenty replicates of drug-free urine were also tested on each day. At 25% above the cutoff, the precision of each assay was as follows: AMP=100%, COC=100%, OPI2= 96.7%, OPI3= 100%, PCP=100% and THC= 95%.

Reproducibility (Amphetamines, Cocaine, Opiates 300, PCP, and THC)

A panel of 55 naturally metabolized human urine samples was prepared. All samples in the panel had been screened for the presence or absence of AMP, COC, PCP and THC. In addition, each of the 55 samples had also been quantitated by GC/MS conducted at SAMHSA cutoffs for positive samples or at limit of quantitation for negative samples to determine the concentration of a specific drug. Five of the 55 samples were drug-free negatives and 50 of the samples were positive for one or more of the five drugs. The concentration of primary metabolite in the positive samples was between 1056 and 4622 ng/mL for AMP; 487 and 1342 ng/mL for COC; 464 and 2000 ng/mL for OPI3; 32 and 109 ng/mL for PCP and 66 and 198 ng/mL for THC. The panel was used to evaluate the lot-to-lot and lab-to-lab reproducibility.

Lot-to-Lot Reproducibility (Amphetamines, Cocaine, Opiates 300, PCP, and THC)

Three aliquots of each of the 55 samples were prepared and each of the three sets of aliquots was coded and used to evaluate the performance of one of three lots of drug tests for the five drugs above. There was one incorrect result (a false negative on an amphetamine low positive sample) on the 825 tests for a reproducibility of >99%.

Lab-to-Lab Reproducibility (Amphetamines, Cocaine, Opiates 300, PCP, and THC)

Three aliquots of each of the 55 samples were prepared and each of the three sets of aliquots was tested by one of three study participants using one lot of the five drug test panel above. There was >99% agreement between the three participants. Overall, there were three incorrect results, two incorrect results for OPI3 (one false negative on an opiate low positive sample and one false negative on an opiate high positive sample) and one incorrect result for PCP (one false negative a low positive sample), on the 825 tests.

Reproducibility (Opiates 2000)

A panel of 25 naturally metabolized human urine samples was prepared. All samples in the panel had been screened for the presence or absence of opiates. In addition, each of the positive samples had also been quantitated by GC/MS conducted at SAMHSA cutoff for positive samples to determine the concentration of morphine and codeine. The concentration of morphine and/or codeine in the positive samples was between 2000 and 6000 ng/mL. The panel was used to evaluate Opiates 2000 for lot-to-lot and lab-to-lab reproducibility. There were no incorrect results on the 75 tests (25 samples x 3 lots) for a lot-to-lot reproducibility of 100%. There were no incorrect results on the 75 tests (25 samples x 3 study participants) for a lab-to-lab reproducibility of 100%.

Accuracy (Propoxyphene)

One-hundred forty one (141) clinical samples were evaluated by the Roche Abuscreen OnLine Propoxyphene assay, using a 300 ng/mL cut off. Sixty (60) samples were found to be negative and eighty-one (81) samples were found to be positive by the Roche method. Three aliquots of each sample were prepared, and assayed by three operators in a masked manner. There was no significant difference in the results obtained by the three operators, therefore the results of all three operators are included in the table. Results of this comparison are as follows:

	<u>OnLine Positive</u>	<u>OnLine Negative</u>
PROFILE-III ER	238	0
PPX (300 ng/mL cutoff)	5	180

* GC/MS results are 390, 441, 499, 536 and 679 ng/mL

In addition to the 141 clinical samples, eight additional clinical samples containing only norpropoxyphene were diluted with drug-free urine in order to obtain an adequate number of samples that had concentrations of drug that were challenging to the cutoff. These eight diluted samples, and the 141 clinical samples described above were analyzed by GC/MS for propoxyphene and norpropoxyphene. The level of quantitation of the GC/MS was 30 ng/mL. Only ten of the samples contained propoxyphene, and each of these samples had norpropoxyphene levels greater than 1,647 ng/mL. As in the study above, three aliquots of the 149 samples were prepared, coded, and assayed by three operators in a masked manner. There was no significant difference in the results obtained by the three operators, therefore the results of all three operators are included in the comparison table.

GC/MS Range (ng/mL)	None detected	150-265	339-450	>472
Number of samples	60	8 (Diluted samples)	7	74
Positive	0	12	19	219
Negative	180	12	2	3

Sensitivity/Precision/Distribution of Random Error (Propoxyphene)

Performance around the specific cut-off of 300 ng/ml for norpropoxyphene was evaluated by testing standard drug solutions diluted in drug-free urine in triplicate on 5 different days by 3 operators. Drug-free urine was also tested on each day. There was no significant difference in the results of the three operators so the results were combined and are shown in the following table.

<u>Conc. (ng/mL)</u>	<u>Number Tested</u>	<u>Norpropoxyphene – Cut-off = 300 ng/mL</u>		<u>% Agreement</u>
		<u>Positive</u>	<u>Negative</u>	
0	45	0	45	100
30	45	0	45	100
75	45	1	44	98
150	45	9	36	80
225	45	16	29	64
300	45	37	8	82
375	45	42	3	93
450	45	44	1	98
600	45	45	0	100

Accuracy (Methamphetamine and MDMA)

A panel of naturally metabolized urine samples was analyzed using the PROFILE-III ER PPX/MAMP-MDMA and the GC/MS assay for methamphetamine and MDMA. The results obtained in the two procedures are shown in the following tables.

GC/MS Methamphetamine (limit of quantitation 50 ng/mL)

PROFILE-III ER MAMP (1000 ng/mL cut-off)		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
	Positive	56	0	56
	<u>Negative</u>	<u>2</u>	<u>56</u>	<u>58</u>
	Total	58	56	114

Overall agreement: >98% (112/114). Samples having discrepant results were analyzed by GC/MS. The false negative samples contained methamphetamine at 1056 ng/mL and at 1136 ng/mL.

GC/MS MDMA (limit of quantitation 50 ng/mL)

PROFILE-III ER MDMA (1500 ng/mL cut-off)		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
	Positive	19	1	20
	<u>Negative</u>	<u>4</u>	<u>57</u>	<u>61</u>
	Total	23	58	81

Percent Agreement of MAMP-MDMA Compared to GC/MS

	<u>POSITIVE</u>	<u>NEGATIVE</u>
MAMP	97% (56/58)	100% (56/56)
MDMA	83% (19/23)	98% (57/58)

Sensitivity/Precision MAMP-MDMA

Performance for methamphetamine and MDMA was evaluated by testing standard drug solutions diluted in drug-free urine in duplicates of 8 drug concentrations on 5 different days by 3 operators. Drug-free urine was also tested on each day. The complete results for both drugs are shown in the tables below.

Methamphetamine Cut-off = 1000 ng/mL					MDMA Cut-off= 1500 ng/mL				
Conc. (ng/mL)	No. Tested	(+)	(-)	% Agreement	Conc(ng/mL)	No. Tested	(+)	(-)	% Agreement
0	30	0	30	100	0	30	0	30	100
100	30	0	30	100	500	30	0	30	100
250	30	0	30	100	750	30	0	30	100
500	30	26	4	87	1000	30	12	18	60
750	30	27	3	90	1250	30	23	7	77
1000	30	28	2	93	1500	30	25	5	83
1250	30	29	1	97	2000	30	30	0	100
1500	30	30	0	100	2500	30	30	0	100
2000	30	30	0	100	3000	30	30	0	100

Reproducibility (MAMP-MDMA)

A panel of 18 spiked human urine samples, comprised of drug-free and drug standard samples, was prepared. The panel was examined by 3 operators, once a day for 5 days. The concentration of methamphetamine and MDMA had been quantitated by GC/MS in each of the 18 samples. There was 100% agreement between the three operators over the 5 day period at 0 ng/mL, 1500 ng/mL (cut-off + 50%) and 2000 ng/mL (cut-off + 100%) for methamphetamine. There was also 100% agreement between the three operators over the 5 day period for 0 ng/mL, 2000 ng/mL (cut-off +33%), 2500 ng/mL (cut-off + 67%) and 3000 ng/mL (cut-off + 100%) for MDMA.

Accuracy (Tricyclic Antidepressants, Barbiturates, Methadone and Benzodiazepines)

The accuracy was evaluated by assaying a coded panel of clinical urine samples containing varying concentrations of drugs and comparing the results to validated methods. A validated HPLC assay measured tricyclic antidepressant levels. Validated GC/MS assays measured barbiturates, methadone and benzodiazepines levels. Results are shown in the following tables.

ACCURACY COMPARED TO GC/MS OR HPLC
(Tricyclic Antidepressants, Barbiturates, Methadone and Benzodiazepines)

DRUG CLASS	Concentration Range (ng/mL)	Number of Samples	PROFILE-III ER Results
Tricyclic Antidepressants	305 – 19224	50	49/50 Positive
	228, 235, 238, 238, 246	5	5/5 Negative

Only one tricyclic antidepressant positive sample containing a combination of nortriptyline and amitriptyline for a combined tricyclic antidepressant concentration of 519 ng/mL tested negative.

DRUG CLASS	Concentration Range (ng/mL)	Number of Samples	PROFILE-III ER Results
Barbiturates	201 – 27776	36	36/36 Positive
	155, 155, 156, 158, 161	5	5/5 Negative
Butalbital	240 - 3814	27	27/27 Positive
	109, 151, 194	3	3/3 Positive
Pentobarbital	264	1	1/1 Positive
Methadone	306 – 70560	57	57/57 Positive
	224, 226, 227, 230, 232	5	5/5 Negative
Benzodiazepines	303 – 30813	57	57/57 Positive
	234, 236, 238, 250, 283	5	5/5 Negative

Additionally, the accuracy was evaluated in comparison to a validated HPLC assay for tricyclic antidepressants and to the Roche Diagnostics Systems, Inc, ABUSCREEN ONLINE[®] assays for barbiturates, methadone and benzodiazepines. A panel of clinical urine samples was analyzed and the results obtained in the procedures were compared. Results are shown in the following tables.

**ACCURACY COMPARED TO THE ROCHE ABUSCREEN ONLINE[®] II OR HPLC ASSAYS
(Barbiturates, Benzodiazepines, Methadone, and Tricyclic Antidepressants)**

**ABUSCREEN ONLINE[®] II Barbiturates Result (Secobarbital)
(300 ng/mL cutoff)**

	<u>Positive</u>	<u>Negative</u>	<u>Total</u>
PROFILE-III ER BAR (200 ng/mL cutoff)	62	0	62
Butalbital Test	<u>0</u>	<u>45</u>	<u>46</u>
	Total	62	45
		62	107

Overall agreement: 100% (107/107).

**ABUSCREEN ONLINE[®] II Benzodiazepines Result
(300 ng/mL cutoff)**

	<u>Positive</u>	<u>Negative</u>	<u>Total</u>
PROFILE-III ER BZO (300 ng/mL cutoff)	57	0	57
Nordiazepam Test	<u>0</u>	<u>45</u>	<u>45</u>
	Total	57	45
		57	102

Overall agreement: 100% (102/102).

**ABUSCREEN ONLINE[®] II Methadone Result
(300 ng/mL cutoff)**

	<u>Positive</u>	<u>Negative</u>	<u>Total</u>
PROFILE-III ER MTD (300 ng/mL cutoff)	55	0	55
Methadone Test	<u>0</u>	<u>45</u>	<u>45</u>
	Total	55	45
		55	100

Overall agreement: 100% (100/100).

HPLC Tricyclic Antidepressants (25 ng/mL limit of quantitation)

	<u>Positive</u>	<u>Negative</u>	<u>Total</u>
PROFILE-III ER TCA (300 ng/mL cutoff)	49	0	49
Desipramine Test	<u>1</u>	<u>45</u>	<u>46</u>
	Total	50	45
		50	95

Overall agreement: 99% (94/95). Only one tricyclic antidepressant positive sample containing a combination of nortriptyline (499 ng/mL) and amitriptyline (20 ng/mL) for a combined tricyclic antidepressant concentration of 519 ng/mL tested negative.

**PERCENT AGREEMENT COMPARED TO ROCHE ABUSCREEN
ONLINE ASSAYS OR HPLC
(Barbiturates, Benzodiazepines, Methadone, and Tricyclic Antidepressants)**

	<u>POSITIVE</u>	<u>NEGATIVE</u>
Barbiturates	100% (62/62)	100% (45/45)
Benzodiazepines	100% (57/57)	100% (45/45)
Methadone	100% (55/55)	100% (45/45)
Tricyclic Antidepressants	98% (49/50)	100% (45/45)

Sensitivity/ Precision/ Distribution of Random Error (Barbiturates, Benzodiazepines, Methadone and Tricyclic Antidepressants)

Performance around the specific cutoff for each drug was evaluated by testing standard drug solutions diluted in drug-free urine in triplicate on 5 different days by 3 operators. Drug-free urine was also tested on each day. Operator-to-operator agreement was excellent, therefore, the data were combined and summarized in the following tables.

Barbiturates (Butalbital) Cutoff = 200 ng/mL

<u>Conc. (ng/mL)</u>	<u>Number Tested</u>	<u>Positive</u>	<u>Negative</u>	<u>% Agreement</u>
Negative	45	0	45	100
50	45	0	45	100
100	45	0	45	100
150	45	12	33	73
200	45	43	2	96
250	45	45	0	100
300	45	45	0	100

Benzodiazepines (Nordiazepam) Cutoff = 300 ng/mL

<u>Conc. (ng/mL)</u>	<u>Number Tested</u>	<u>Positive</u>	<u>Negative</u>	<u>% Agreement</u>
Negative	45	0	45	100
30	45	0	45	100
75	45	6	39	87
150	45	27	18	60
225	45	41	4	91
300	45	42	3	93
375	45	43	2	96
450	45	45	0	100
600	45	45	0	100

Methadone (Methadone) Cutoff = 300 ng/mL

Conc. (ng/mL)	Number Tested	Positive	Negative	% Agreement
Negative	45	0	45	100
30	45	3	42	93
75	45	28	17	62
150	45	35	10	78
225	45	43	2	96
300	45	45	0	100
375	45	45	0	100
450	45	43	2	96
600	45	44	1	98

Tricyclic Antidepressants (Desipramine) Cutoff = 300 ng/mL

Conc. (ng/mL)	Number Tested	Positive	Negative	%Agreement
Negative	45	0	45	100
30	45	2	43	96
75	45	17	28	62
150	45	33	12	73
225	45	34	11	76
300	45	40	5	89
375	45	41	4	91
450	45	44	1	98
600	45	45	0	100

Unrelated Compounds, Prescription and Over-the-Counter Medications

The following compounds were tested for reactivity. Listed compounds were dissolved in appropriate solvents and then added to drug-free urine for testing. Unless otherwise noted, all of the listed compounds were negative in each of the tests at 100µg/mL. If a drug name is followed by an abbreviation such as "AMP" or "BAR" etc., check the "Related Compounds and Cross Reactants" listing for the drug in question under the appropriate heading (AMP, BAR, etc.) The drug may not cause a presumptive positive drug screen for that drug class.

Acecaïnide (N-Acetylprocainamide)	Dexamethasone	I-11-Hydroxy- Δ^9 -THC-THC
Acetaminophen	Dextromethorphan	Hydroxyhippuric Acid
Acetylsalicylic Acid	Diacetylmorphine-OPI	p-Hydroxyphenobarbital-BAR
Allobarbital-BAR	Diazepam-BZO	4-Hydroxyphenacylidine-PCP
Alphenal-BAR	Diclofenac	3-Hydroxytyramine
Alprazolam-BZO	Diethylpropion	Hydroxyzine
Alprazolam, 1-Hydroxy-BZO	Diflunisal	Ibuprofen
p-Aminobenzoic Acid	Digoxin	Imipramine -TCA
7-Aminoclonazepam-BZO	Dihydrocodeine-OPI	Iproniazid
7-Aminoflunitrazepam-BZO	Dimenhydrinate (Dramamine)	(R)-Isoproterenol
Aminoglutethimide-BAR	1,3-Dimethylbarbituric acid-BAR	Isoxsuprine
I-Aminopyrine (4-(dimethylamino) antipyrine)	Diphenhydramine	Ketamine
Amitriptyline-TCA	Diphenylhydantoin (Phenytoin)-BAR	Ketoprofen
Amobarbital-BAR	Domperidone	Labelalol
Amoxapine	Dopamine	Levorphanol-OPI
Amoxicillin	Doxepin-TCA	Lidocaine
d-Amphetamine-AMP, MAMP	Doxylamine	Lithium carbonate
l- Amphetamine-AMP, MAMP	Ecgonine-COC	Loperamide
Ampicillin	Ecgonine Methyl Ester-COC	Lorazepam-BZO
Apomorphine-OPI	EDDP-(Primary metabolite of methadone)-MTD	Lorazepam glucuronide-BZO
l-Ascorbic Acid	Efavirenz (Sustiva)	Loxapine- TCA
Aspartame	EMDP-(Secondary metabolite of methadone)-MTD	Lysergic Acid
Atenolol	Ephedrine-AMP, MAMP	Lysergic Acid Diethylamide (LSD)
Atomoxetine	Equilin	Maprotiline-TCA
Atropine Sulfate	Erythromycin	MDA-AMP, MAMP
Barbital-BAR	Estrone	MDE (MDEA)-AMP, MAMP
Barbituric Acid-BAR	Ethanol	MDMA-AMP, MAMP
Benzilic Acid	Ethylmorphine-OPI	Melanin
Benzoic Acid	Fenfluramine-MAMP	Meperidine
Benzocaine (ethyl-4-aminobenzoate)	Fenpropofen	Mephobarbital-BAR
Benzoyllecgonine-COC	Fentanyl (Synthetic opiate)	Mepivacaine
Benzphetamine	Flunitrazepam-BZO	Mesoridazine
Benztropine	Fluoxetine (Prozac)	Methadone-MTD
Brompheniramine	Flurazepam-BZO	d-Methamphetamine-AMP, MAMP
Buprenorphine (Methadone replacement)	Fluvoxamine	l-Methamphetamine- AMP, MAMP
Bupropion	Furosemide	Methaqualone
Butabarbital-BAR	Gentisic Acid (2,5-Dihydroxybenzoic acid)	Methcathinone
Butalbital-BAR	Glutethimide-BAR	Methocarbamol
Caffeine	Guaiacol Glyceryl Ether	Methoxyphenamine
Cannabidiol-THC	Haloperidol	Methylphenidate
Cannabinol-THC	Hexobarbital-BAR	Methylprylon
Captopril	Hippuric acid	Metoprolol
Carbamazepine- TCA	Hydralazine	Midazolam-BZO
Carbamazepine-10,11 epoxide- TCA	Hydrochlorothiazide	Mirtazapine- TCA
Carisoprodol (Meprobamate)	Hydrocodone-OPI	6-Monoacetylmorphine-OPI
Cephalexin	Hydrocortisone	Morphine-OPI
Chloral Hydrate (Norchlordiazepoxide)-BZO	Hydromorphone-OPI	Morphine 3- β -D-Glucuronide-OPI
Desmethylflunitrazepam-BZO	Hydroxybupropion	Morphine 6- β -D-Glucuronide-OPI
Desmethylvenlafaxine		Nalidixic Acid

Naltrexone- OPI	Pentobarbital- BAR	Selegiline (Deprenyl)
Nalorphine- OPI	Perphenazine- TCA	Serotonin (5-Hydroxytryptamine)
Naloxone- OPI	Phenacetin (Acetophenetidin)	Sertraline (Zoloft)
Naproxen	Phencyclidine- PCP	Sildenafil (Viagra)
Niacinamide	Phendimetrazine	Sulfamethazine
Nicotine	Phenelzine	Sulindac
Nifedipine	Phenethylamine- AMP, MAMP	Talbutal- BAR
Nitrazepam- BZO	Pheniramine	Temazepam- BZO
Nitrofurantoin	Phenmetrazine	Temazepam glucuronide- BZO
Norclomipramine- TCA	Phenobarbital- BAR	Tetracycline
Norcodeine- OPI	Phenothiazine- TCA	Δ^9 -Tetrahydrocannabinol- THC
Nordiazepam- BZO	Phentermine- AMP, MAMP	Δ^8 -Tetrahydrocannabinol- THC
Nordoxepin- TCA	Phenytoin (Diphenylhydantoin)- BAR	Tetrahydrozoline
Norethindrone	Phenylbutazone	Thebaine- OPI
Norlysergic Acid	Phenylephrine	Theopylline
Normeperidine	Phenylpropanolamine	Thiamine
Norpropoxyphene- PPX	Piroxicam	Thiopental
l-Norpseudoephedrine	Prazosin	Thioridazine
Nortriptyline- TCA	Prednisolone	Thiothixene- TCA
Noscapine	Prednisone	Tolbutamide
Nylidrin	Procaine	Tolmetin (Tolectin)
Octopamine	Procaainamide	Trazodone
Ofloxacin	Prochlorperazine	Triamterene
Olanzapine- TCA	Promazine- TCA	Triazolam- BZO
Omeprazole	Promethazine	Triazolam, 1-hydroxy- BZO
Orphenadrine	Propoxyphene- PPX	Trifluoperazine
Oxalic Acid	Propranolol	Trimethoprim
Oxaprosin	Protriptyline- TCA	Trimipramine- TCA
Oxazepam- BZO	Pseudoephedrine- MAMP	Tripelennamine
Oxazepam glucuronide- BZO	Pyrilamine	Tryptamine
Oxolinic Acid	Quetiapine (Seroquel)- TCA	Tryptophan
Oxycodone- OPI	Quinidine	Tyramine- AMP,MAMP
Oxymetazoline	Ranitidine	Tyrosine
Oxymorphone- OPI	Riboflavin	Valproic Acid
Papaverine hydrochloride	Rifampin	Venlafaxine
Penicillin G	Salicylic Acid	Verapamil
Pentazocine	Secobarbital- BAR	Zomepirac

Non Crossreactive Endogenous Compounds

Fifteen compounds were dissolved in appropriate solvents at a concentration of at least 1.0 mg/mL. Each compound was further diluted to 100 µg/mL except for albumin (20 mg/mL) and bilirubin (200 µg/mL). None of these compounds showed cross-reactivity at the listed concentrations.

Acetaldehyde	Creatinine	Hemoglobin, Human
Acetone	Epinephrine	Sodium Chloride
Albumin, Human	β-Estradiol	Tetrahydrocortisone
Bilirubin	Estriol	d,1-Thyroxine
Cholesterol	Glucose Std. Solution	Uric Acid

Related Compounds and Cross Reactants

The following metabolites and compounds were tested. Reference standards for the various metabolites and compounds were prepared in negative urine samples. None of the compounds reacted with the remaining tests in the panel. Results are expressed as the minimum concentration required to produce a positive result in the indicated assay.

Amphetamines- (AMP)(d-Amphetamine) 1000 ng/mL

I-Amphetamine	Result
Ephedrine	Positive at 100 µg/mL
MDA	Negative at 100 µg/mL
MDMA	Positive at 400 ng/mL
MDE (MDEA)	Negative at 100 µg/mL
I-Methamphetamine	Negative at 100 µg/mL
d-Methamphetamine	Negative at 100 µg/mL
Phenethylamine	Negative at 100 µg/mL
Phentermine	Positive at 10 µg/mL
Tyramine	Negative at 100 µg/mL

Barbiturate-(BAR) (Butalbital) 200 ng/mL

Allobarbitol	Result
Alphenal	Positive at 500 ng/mL
Amino glutethimide	Positive at 100 ng/mL
Amobarbital	Negative at 100,000 ng/mL
Barbital	Positive at 2500 ng/mL
Barbituric Acid	Positive at 2500 ng/mL
Butabarbital	Negative at 100,000 ng/mL
Cyclopentobarbital	Positive at 750 ng/mL
1,3 Dimethylbarbituric Acid	Positive at 250 ng/mL
Diphenylhydantoin (Phenytoin)	Negative at 100,000 ng/mL
Glutethimide	Negative at 100,000 ng/mL
Hexobarbital	Negative at 100,000 ng/mL
p-Hydroxyphenobarbital	Positive at 500 ng/mL
Mephobarbital	Negative at 100,000 ng/mL

Barbiturate-(BAR) (Butalbital) 200 ng/mL

Pentobarbital	Result
Phenobarbital	Positive at 500 ng/mL
Secobarbital	Positive at 800 ng/mL
Talbutal	Positive at 75 ng/mL
	Positive at 50 ng/mL

Benzodiazepine-(BZO) (Nordiazepam) 300ng/mL

Alprazolam	Result
Alprazolam, 1-OH	Positive at 250 ng/mL
7-Aminoclonazepam	Positive at 25 µg/mL
7-Aminoflunitrazepam	Negative at 100 µg/mL
Chlordiazepoxide	Negative at 100 µg/mL
Clobazam	Positive at 50 ng/mL
Clonazepam	Positive at 250 ng/mL
Clorazepate	Positive at 250 ng/mL
Desalkylflurazepam	Positive at 250 ng/mL
Desmethylchlordiazepoxide	Positive at 500 ng/mL
Desmethylflunitrazepam	Positive at 75 ng/mL
Diazepam	Positive at 50 ng/mL
Flunitrazepam	Positive at 75 ng/mL
Flurazepam	Negative at 100 µg/mL
Lorazepam	Positive at 2.5 µg/mL
Lorazepam glucuronide	Positive at 1 µg/mL
Midazolam	Positive at 5 µg/mL

Benzodiazepine-(BZO) (Nordiazepam) 300ng/mL

Nitrazepam	Positive at 50 ng/mL
Oxazepam	Positive at 500 ng/mL
Oxazepam glucuronide	Positive at 2.5 µg/mL
Temazepam	Positive at 50 ng/mL
Temazepam glucuronide	Positive at 750 ng/mL
Triazolam	Positive at 750 ng/mL
Triazolam, 1-OH	Negative at 10 µg/mL

Cocaine-(COC) (Benzoylcegonine) 300 ng/mL

Cocaine	Positive at 100 ng/mL
Ecgonine	Positive at 75 µg/mL
Ecgonine Methyl Ester	Negative at 100 µg/mL

Methadone-(MTD) (Methadone) 300 ng/mL

Primary metabolite (EDDP)	Negative at 100 µg/mL
Secondary metabolite (EMDP)	Negative at 100 µg/mL

Methamphetamine-(MAMP) (d-Methamphetamine) 1000 ng/mL,
(MDMA) 1500 ng/mL

d-Amphetamine	Negative at 100 µg/mL
l-Amphetamine	Negative at 100 µg/mL
Ephedrine	Positive at 2.5 µg/mL
Fenfluramine	Positive at 25 µg/mL
MDA	Negative at 100 µg/mL
MDE (MDEA)	Positive at 5 µg/mL
l-Methamphetamine	Positive at 7.5 µg/mL
Phenethylamine	Positive at 2.5 µg/mL
Phentermine	Negative at 100 µg/mL
Pseudoephedrine	Negative at 100 µg/mL
Tyramine	Negative at 100 µg/mL

Opiates(2000)-(OPI) (Codeine and Morphine) 2000ng/mL

Apomorphine	Negative at 100 µg/mL
Diacetylmorphine	Positive at 2.0 µg/mL
Dihydrocodeine	Positive at 3 µg/mL
Ethylmorphine	Positive at 400 ng/mL
Hydrocodone	Positive at 2.0 µg/mL
Hydromorphone	Positive at 3 µg/mL
Levorphanol	Positive at 12.5 µg/mL
6-Monoacetyl Morphine	Positive at 3 µg/mL
Morphine 3-β-D-Glucuronide	Positive at 3 µg/mL
Morphine 6-β -D-Glucuronide	Positive at 25 µg/mL
Nalorphine	Negative at 100 µg/mL
Naloxone	Negative at 100 µg/mL
Naltrexone	Negative at 100 ug/mL
Norcodeine	Positive at 25 µg/mL
Oxycodone	Negative at 100 µg/mL
Oxymorphone	Negative at 100 µg/mL
Thebaine	Positive at 50 µg/mL

Interference Propoxyphene/Methamphetamine Only

Following the study of M.L. Smith, et. al. the following drugs were tested to determine the degree of interference they may have on the test. Commercial negative urine was spiked with 100 µg/mL of each of these drugs and with either 75 ng/mL or 600 ng/mL of norpropoxyphene or methamphetamine. Each spiked sample was tested in triplicate on the test. None of these drugs affected the expected negative or positive results with either the 75 ng/mL or 600 ng/mL fortified samples. The drugs are listed below.

Acetylsalicylic Acid	Chlorpheniramine	Ibuprofen
Acetaminophen	Cocaine	Morphine
Brompheniramine maleate	Dextromethorphan	Phenobarbital
Caffeine	5,5 Diphenylhydantoin	d-Pseudoephedrine
Carbamazepine	Doxylamine	Salicylic Acid

Opiates(300)-(OPI) (Codeine and Morphine) 300ng/mL

Apomorphine	Negative at 100 µg/mL
Diacetylmorphine	Positive at 200 ng/mL
Dihydrocodeine	Positive at 400 ng/mL
Ethylmorphine	Positive at 200 ng/mL
Hydrocodone	Positive at 800 ng/mL
Hydromorphone	Positive at 800 ng/mL
Levorphanol	Negative at 100 µg/mL
6-Monoacetylmorphine	Positive at 200 ng/mL
Morphine 3-β-D-Glucuronide	Positive at 200 ng/mL
Morphine 6-β-D-Glucuronide	Positive at 12.5 µg/mL
Nalorphine	Positive at 75 µg/mL
Naloxone	Negative at 100 µg/mL
Naltrexone	Negative at 100 µg/mL
Norcodeine	Positive at 12.5 µg/mL
Oxycodone	Negative at 100 µg/mL
Oxymorphone	Negative at 100 µg/mL
Thebaine	Positive at 12.5 µg/mL

Phencyclidine-(PCP) (Phencyclidine) 25 ng/mL

4-Hydroxyphencyclidine	Positive at 5 µg/mL
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Propoxyphene-(PPX)(Norpropoxyphene) 300 ng/mL

Propoxyphene	Positive at 50 ng/mL
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Cannabinoids-(THC) (11-nor-9-carboxy-Δ⁹-THC) 50 ng/mL

Cannabidiol	Negative at 100 µg/mL
Cannabinol	Negative at 100 µg/mL
l-11 Hydroxy-Δ ⁹ -THC	Negative at 50 µg/mL
Δ ⁹ -Tetrahydrocannabinol	Negative at 100 µg/mL
Δ ⁹ -Tetrahydrocannabinol	Negative at 100 µg/mL

Tricyclic Antidepressant-(TCA) (Desipramine) 300 ng/mL

Amitriptyline	Positive at 500 ng/mL
Carbamazepine	Negative at 100 µg/mL
Carbamazepine-10, 11 epoxide	Negative at 100 µg/mL
Chlorpromazine	Negative at 100 µg/mL
Chlorprothixine	Negative at 100 µg/mL
Clomipramine	Negative at 100 µg/mL
Clozapine	Positive at 2.5 µg/mL
Cyclobenzaprine	Positive at 750 ng/mL
Doxepin	Positive at 750 ng/mL
Imipramine	Positive at 250 ng/mL
Loxapine	Negative at 100 µg/mL
Maprotiline	Positive at 750 ng/mL
Mirtazapine	Negative at 100 µg/mL
Norclomipramine	Negative at 100 µg/mL
Nordoxepin	Positive at 500 ng/mL
Nortriptyline	Positive at 500 ng/mL
Olanzapine	Positive at 75 µg/mL
Perphenazine	Negative at 100 µg/mL
Phenothiazine	Negative at 100 µg/mL
Promazine	Positive at 250 ng/mL
Protriptyline	Negative at 100 µg/mL
Thiothixene	Negative at 100 µg/mL
Trimipramine	Positive at 5 µg/mL
Quetiapine (Seroquel)	Positive at 5 µg/mL

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16. LIMITED EXPRESS WARRANTIES

The manufacturer makes no express warranty other than the diagnostic test kit will measure certain drugs and/or drug metabolites when used in accordance with the manufacturer's printed instructions. The use of the kit for any other purpose is outside the intended use of this product. The manufacturer gives no express warranty as to what the legal or clinical significance is of the levels of drug(s)/drug metabolites detected by the PROFILE-III ER Drugs of Abuse Test. The manufacturer disclaims any and all implied warranties of merchantability, fitness for use or implied utility for any other purposes. Any and all damages for failure of the kit to perform to its instructions are limited to the replacement value of the kit.

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U.S. Patent Nos. 5,202,268, 6,566,051, 6,376,251

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